recitation "R "is explicitly said to be an "alkyl, > CH_3". Moreover, through out the whole of the application, the code used for amino acids is constantly and consistently the three-letter code. There is no mention to be found in the content of the application, of amino acid coding using the one-letter code. Therefore, the recitation "(N-R) aa" unambiguously refers to an amino acid bearing an R radical on its nitrogen atom.

Similarly, the recitation "(R) Val" in claim 16 clearly refers to a valine having an R radical bound to its nitrogen: claim 16 depends from claim 15, and therefore, the Z residue is the same as in claim 15, namely, an N-substituted amino acid, where the amino acid is valine, and the R is conjugated to the nitrogen.

Claim rejections under 35 USC 102

Claims 15, 16 and 18-21 were rejected under 35 USC 102.

This objection is respectfully traversed.

The Applicant is of the opinion that none of claims 15-21 are anticipated by Steiner et al. (US 6 444 643).

In this disclosure, all the cyclosporines described have an N-methylated amino acid as the residue in position 4 (col. 3, line 18; Formula II; col. 10, line 13). In other words, the fourth residue has its nitrogen substituted with a methyl group. By contrast, in present claim 15, the fourth residue (Z) is an amino acid with an R substitution on the nitrogen, R being an alkyl > CH_3. This recitation clearly rules out the possibility of a methyl substitution.

The Examiner further mentioned the passage col. 11; line 18 in Steiner et al. This section certainly deals with "N-alkylation", but the Applicant respectfully submits that this

citation does not relate at all to the subject-matter claimed by Steiner et al. On the contrary, this N-alkylation is mentioned there to briefly discuss some prior art, and not to further describe their invention. Hence, it is improper to combine this feature with the rest of the description. In particular, Steiner et al. do not disclose a cyclosporine with one part as in formula IV, and another part as in another piece of prior art.

As a conclusion, Steiner et al. fail to disclose a cyclosporin which has, as the fourth residue, an amino acid with its nitrogen being substituted by an alkyl group higher than a methyl.

Therefore, the presently claimed subject-matter is not anticipated by the disclosure of Steiner et al.

Claim rejections under 35 USC 103

Claims 15-21 were objected to, as being obvious over Ko et al. together with Steiner et al.

This rejection is respectfully traversed.

The Steiner et al. disclosure neither teaches, nor suggests a cyclosporin as in present claim 15. The same applies to the Ko et al. disclosure, where the 4th residue is always N-methylated. Therefore, the presently claimed subject matter is indeed non-obvious to the person of ordinary skill in the art.

In addition, the Applicant would like to point out that Steiner et al. relates to neurological activity, and fails to mention an HIV-related application.

Moreover, as indicated on several occasions in the present application (page 3, line 18; page 5, line 11), the new cyclosporins according to the invention not only possess an improved anti-HIV activity, but also, and very surprisingly, do not exhibit the immunosuppressive activity of the other known cyclosporins. Knowing that HIV is an immunosuppressive disease, it is absolutely crucial to lower the immunosuppressive effect of any drug that is given as a treatment for HIV. It was absolutely unexpected and totally non-obvious for the person ordinarily skilled in the art that the N-alkylation with an alkyl group higher than methyl on the fourth residue, would lead to such beneficial effects.

Therefore, present claims are non-obvious over the cited prior art.

In view of the foregoing it is respectfully submitted that the application is now in proper form for allowance.

Respectfully submitted.

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Date June 23, 2003 By: Michael O. Sturm

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